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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/701,265

11/04/2003

Brenda F. Baker

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EXAMINER

PITRAK, JENNIFER S

ART UNIT

PAPER NUMBER

1635

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/701,265	Applicant(s) BAKER ET AL.	
	Examiner Jennifer Pitrak	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 November 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 120-167 is/are pending in the application.
- 4a) Of the above claim(s) 125, 126, 128-135, 141, 142, 144-147 and 150-167 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 120-124, 127, 136-140, 143, 148 and 149 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>See Continuation Sheet</u> | 6) <input type="checkbox"/> Other: _____ |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :01/06/04; 04/30/04; 08/11/04; 09/13/04; 01/13/05; 01/26/05; 03/14/05; 03/18/05; 04/04/05; 04/15/05; 11/03/06; 11/20/07.

DETAILED ACTION

Election/Restrictions and Claims Status

Applicant's election without traverse of Group I, drawn to compositions comprising chimeric oligomers in the reply filed on 11/20/07 is acknowledged. Group I originally encompassed claims 1-119. Claims 1-119 have been cancelled. Claims 120-167 have been added and read on Group I.

Applicant's election without traverse of the following species in the reply on 11/20/07 is acknowledged: gapmer(s) containing wings with 2'-OCH₃ modified nucleosides and the gap containing ribonucleosides and the internucleoside linkages are mixed phosphodiester and phosphorothioate.

Claims 125, 126, 128-135, 141, 142, 144-147, and 150-167 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/20/07.

Claims 120-124, 127, 136-140, 143, 148, and 149 are currently under examination.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: The later-filed application must be an application for a patent for an invention that is also disclosed in the prior application (the parent or original nonprovisional application or provisional

application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, Application No. 10/078,949 and 60/423,760, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Applications '949 and '760 do not provide support for compositions comprising two 17-25-nucleobase oligomers comprising at least 17 contiguous nucleobases of 100% complementarity. Application '949 provides support for a blunt-ended oligomeric RNA duplex that consists of two 17-nucleotide strands, wherein one strand is a gapmer, wherein the strands are 100% complementary over the entire 17-nucleotides (example 25 on page 89 of the 10/078,949 application). Such a duplex was presented in Application '949 as a test substrate for RNaseH. Support for compositions comprising complementary duplexes comprising 17 contiguous nucleobases of 100% complementarity is first provided in the 11/20/07 amendment to the instant application. Thus, claims 120-124, 127, 136-138 are afforded the benefit of the instant application filed 11/04/03.

Claim Objections

Claim 122 is objected to because of the following informalities: the claim refers to a single 5' end and a single 3' end of the claimed duplex, but the duplex necessarily consists of two 5' ends and two 3' ends. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 120-124, 127, and 136-138 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

Claim 120 recites "at least 17 contiguous nucleobases of the first chemically synthesized oligomeric compound are 100% complementary to at least 17 contiguous nucleobases of the second chemically synthesized oligomeric compound." This limitation was first introduced into the claims in the amended claims filed on 11/20/07 and no support for this amendment is present in the instant specification. Therefore, this limitation constitutes new matter. Claims 121-124, 127, 136-138 are rejected because they depend from claim 120.

Should applicants disagree, applicants are encouraged to specifically point out by page and line number(s) where such support may exist for each claim limitation added in the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 120, 121, 123, 124, 127, and 136-138 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Crooke (2000, U.S. Patent 6,107,094).

The claims are to a composition comprising a duplex of two chemically synthesized oligomeric compounds wherein each compound consists of 17-25 linked nucleosides; at least 17 contiguous nucleobases of the first compound are 100% complementary to at least 17 contiguous nucleobases of the second compound; the first compound is a gapmer, wherein the gap consists of at least four ribonucleosides and the wings consist of from two to seven 2'-OCH₃ modified nucleosides; at least one of the compounds comprises at least one phosphorothioate linkage ; both compounds comprise at least one phosphorothioate linkage (claims 120, 124, 127, 136, 137, 138). The claims are further drawn to the compound of claim 120 wherein both compounds are gapmers with at least a 4-nucleoside gap and 2'-OCH₃-modified wings (claim 121) or wherein the duplex of claim 120 is blunt-ended (comprises no overhanging nucleotides) (claim 123).

Crooke teaches a blunt-ended 17-ribonucleoside duplex with 100% complementarity wherein one strand of the duplex is RNA and the other strand is a gapmer consisting of 4-nucleotide phosphorothioate-linked 2'-OCH₃ wings and a 9-nucleotide phosphodiester-linked RNA gap (Example 25, p.89). In example 28 on p.99, Crooke teaches duplexes in which both strands contained flanking regions comprised of 2'-OCH₃ nucleosides and phosphorothioate linkages. Thus, Crooke anticipates the instant claims 120, 121, 123, 124, 127, and 136-138.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 120-124, 127, 136-138 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crooke (2000) as applied to claims 120, 121, 123, 124, 127, 136-138 above, and further in view of Elbashir, *et al.* (2001, item 42 on 11/20/07 IDS).

Claims 120, 121, 123, 124, 127, 136-138 are to the compositions as described above. Claim 122 is to the composition of claim 120 wherein the duplex comprises an overhang on the 5' end, on the 3' end, or on both the 5' end and the 3' end.

Crooke teaches a composition comprising a 17-base-pair RNA duplex as described above and that the oligomeric compounds of his invention are useful for modulating the expression of a protein (abstract). Crooke teaches that the ability of the RNA gapmer compounds to reduce mRNA depended on the size of the RNA gap and that at least a 4-nucleotide gap was required for cleavage of the target RNA (first paragraph, column 47). Crooke does not teach the duplex comprising any nucleotide overhangs, nor does he teach the use of the duplex molecules for targeting RNA cleavage.

Elbashir, *et al.* teach siRNAs, which are duplexes of 21-23 nucleotide RNAs and are the mediators of RNA interference (RNAi), a sequence-specific mechanism of targeted RNA degradation (abstract and first paragraph of Introduction). The authors performed systematic analysis of the length, secondary structure, sugar backbone, and the sequence specificity of siRNA duplexes for RNAi (bottom of first column, p.6878). The authors teach that duplexes of 21 nucleotide siRNAs with 2-nucleotide 3' overhangs were more efficient triggers of RNAi than were blunt-ended siRNAs (Figure 1, p. 6879) and that substitution of one or both strands by 2' -

O-methyl oligonucleotides abolished RNAi, but that multiple substitutions at the 3' end were tolerated (abstract; Fig. 4, p.6882).

It would have been obvious to one skilled in the art at the time of the instant application to make a composition comprising a gapped duplexed RNA as described by Crooke, *et al.*, wherein the duplex further comprised overhangs at either or both the 3' and 5' ends, herein referred to as a "gapped siRNA". One would have been motivated to make the gapped siRNA because Crooke teaches that a gapmer oligonucleotide containing a gap of at least 4 nucleotides was effective at initiating target RNA cleavage and Elbashir, *et al.* demonstrate that 2-nucleotide 3' overhangs make siRNA molecules more efficient RNAi triggers than blunt-ended duplexes. One would expect to succeed at making gapped siRNAs because both gapped RNA duplexes and siRNAs were known and previously made and the modifications in the gapped RNA duplex of Crooke were known to impart greater stability to RNA. Thus, the instant claims would have been obvious to one skilled in the art at the time of the instant application.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 139, 140, 143, 148, and 149 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4, 7, and 8 of U.S. Patent No. 6,107,094 ('094) and over claim 29 or U.S. Patent 5,898,031. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are to species encompassed by the generic claims of '094 and are anticipated by claim 29 of '031. Furthermore, the disclosure of '094 teaches an antisense gapmer ('9 base RNA gap" in Figure 1 and column 8) that meets the limitations of the instant claims.

The following serial numbers are of co-pending applications that contain claims drawn to similar subject matter, and against which a provisional obviousness-type double patenting rejection may be appropriate: 10/860,455; 10/909,125; 10/664,639; 10/701,007; 10/701,264; 10/701,285; 10/936,273; 10/561,618; 10/700,689; 10/700,697; 10/701,236; 10/701,316; 10/860,265; 11/054,848; 10/561,324; 11/226,882; 11/565,781; 11/565,770; 11/565,773; 11/565,794; 11/565,799; 11/565,804; 11/565,817; 11/565,823; 11/565,833; 11/565,839; 11/565,858; 11/565,816; 11/565,841; 11/569,929; 11/747,042; 11/569,931; 11/569,939; 11/569,941; 11/569,955.

Applicant is encouraged to review all applications and file terminal disclaimers as necessary. Furthermore, it is Applicant's duty to disclose any pending applications or patents, which are not listed above, and to submit an appropriate terminal disclaimer over these applications or patents as pertinent to the instant invention.


Closing

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Pitrak whose telephone number is 571-270-3061. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Pitrak
Examiner
Art Unit 1635


Examiner, AU 1635